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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/352,466	07/13/1999	VIRGINIA C BROUDY	A-195CDDC	2305

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EXAMINER	
BLANCHARD, DAVID J	

ART UNIT	PAPER NUMBER
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/352,466	BRODY ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *71-73 and 75-92* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *71-73 and 75-92* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 30 April 2009 has been entered.

2. Claims 1-70 and 74 are cancelled.

Claims 71-73 have been amended.

3. Claims 71-73 and 75-92 are pending and under consideration.

4. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.

Rejections Maintained

5. The rejection of claims 71-73 and 75-92 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating leukemia cells comprising administering a therapeutic agent conjugated to the monoclonal antibody produced from the hybridoma cell line ATCC No. HB 10716 (i.e., monoclonal antibody SR-1) or antigen-binding fragments thereof, wherein the monoclonal antibody or antigen-binding fragments thereof bind the human c-kit receptor and blocks binding of human stem cell factor, does not reasonably provide enablement for a method of treating just any cancer comprising administering to a patient a therapeutic agent conjugated to just any monoclonal antibody or fragment thereof that binds human c-kit and blocks binding of human stem cell factor is maintained. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The response filed 4/30/2009 states that the specification clearly teaches how to make antibodies which bind human c-kit and block binding of human stem cell factor to human c-kit, including Example 1, which states that "any cell displaying SCF receptors [c-kit] could be used as an immunogen to elicit antibodies to the SCF receptor [c-kit] (pg.

30, lines 12-13) and a list of exemplary cells and cell lines is provided. The cells and cell lines are available from public depositories such as the ATCC or prepared using known techniques. Procedures for preparing and screening hybridomas which produce antibodies that bind to human c-kit were routine in the art at the time and the specification teaches an assay to determine whether a given c-kit antibody will inhibit binding of stem cell factor to c-kit as described in Example 5. Applicant acknowledges the examiner's citation of the statement at pg. 2, line 15 of the specification , but argues that although there had been no previous reports of antibodies raised against c-kit which blocked SCF binding, this fact by itself doesn't mean that Applicants' must be restricted to only their specific antibody. Applicant argues that the instant disclosure allows one to make additional antibodies. Applicant refers to the cited art of Ashman et al and argues that the functional differences between the three antibodies (SR-1, YB5.B8 and 17F11) merely reflect the fact that antibodies YB5.B8 and 17F11 recognize a different epitope on c-kit and is not evidence of lack of enablement. Applicant asserts that the examiner has not pointed out why one skilled in the art following the specification would require undue experimentation to make and use the claimed antibodies, which block SCF binding to c-kit. Applicant further states that the rejection focuses on the presence of a single working example in the specification along with an unsupported allegation that there is a lack of direction and guidance for preparing other antibodies which bind c-kit and block binding of SCF. Applicants' arguments have been fully considered but are not found persuasive. Applicants' arguments that the specification teaches how to make antibodies which bind human c-kit and block binding of human stem cell factor to human c-kit through the disclosure of available cells displaying SCF receptors, art recognized procedures for producing and screening hybridomas and an assay for determining whether a given c-kit antibody will inhibit binding of stem cell factor to c-kit are not persuasive because the issue is make and use, not make and test to see if the skilled artisan could use. The instant application essentially calls for the use of trial and error to attempt to find an antibody that will block binding of human stem cell factor to human c-kit. A patent is not a reward for a search, but compensation for its successful conclusion. Reasonable detail must be provided in order to enable members of the public to understand and carry out

the invention. In short, the instant application describes a method for determining whether a given antibody possesses certain desired characteristics, however, without more precise guidelines, amount to little more than "a starting point, a direction for further research." *Genentech*, 108 F.3d at 1366. *See also Calgene*, 188 F.3d at 1374 ("the teachings set forth in the specification provide no more than a 'plan' or 'invitation' for those of skill in the art to experiment practicing [the claimed invention]; they do not provide sufficient guidance or specificity as to how to execute that plan"); *National Recovery Technologies*, 166 F.3d at 1198 (stating that patent-in-suit "recognizes a specific need… and suggests a theoretical answer to that need. It provides a starting point from which one of skill in the art can perform further research in order to practice the claimed invention, but this is not adequate to constitute enablement"). The instant specification does not describe the claimed invention in terms that will "enable any person skilled in the art… to make and use" the invention commensurate in scope with the claims. At most, the specification will enable a person of ordinary skill in the art to attempt to discover how to practice the claimed invention.

Further, the state of the prior art as well as applicants' disclosure indicates that simply following the teachings in the specification to produce a monoclonal antibody that binds human c-kit and blocks binding of human stem cell factor to human c-kit would have been an unpredictable at the time of filing since the "role of c-kit in cancer is somewhat ambiguous" pg. 69, 1st col. of Lennartsson et al (Current Cancer Drug Targets, 6:65-75, 2006, cited on PTO-892 mailed 6/28/06) and a*ccording to applicants' specification, the prior art has not been able to obtain a monoclonal antibody to the c-kit receptor with any expectation that such a monoclonal antibody would possess the ability to block the binding of the c-kit ligand, stem cell factor (see specification at pg. 2)* indicating a high degree of unpredictability. Further, the art of Ashman et al (J. Cell Physiol. 158:545-554, 1994, Exhibit A in the reply filed 12/29/05 teach three different monoclonal antibodies to the human c-kit receptor. Monoclonal antibody SR-1 potentially blocked the binding of stem cell factor to the human c-kit receptor on HEL-DR and MO7e cells, whereas monoclonal antibodies YB5.B8 and 17F11 had minimal

effects on ligand binding. Further, SR-1 potently inhibited the proliferative response to stem cell factor, while 17F11 weakly inhibited and YB5.B8 had negligible effect.

The examiner acknowledges that the presence of only one working example should never be the sole reason for rejecting claims as being broader than the enabling disclosure, even though it is a factor to be considered along with all the other factors as in the instant rejection. To make a valid rejection, one must evaluate all the facts and evidence and state why one would not expect to be able to extrapolate that one example across the entire scope of the claims. As set forth in the rejection, the specification teaches that monoclonal antibody SR-1 was produced by immunization of mice with cells of the OCIM1 line, however, as discussed supra immunization of mice with OCIM1 cells or any cells known to express human c-kit will not necessarily or predictably reproduce a monoclonal antibody possessing the properties of monoclonal antibody SR-1, particularly in view of the state of the prior art. Importantly, the specification does not define or characterize the epitope of human c-kit to which the SR-1 antibody binds. There is insufficient guidance and direction to assist the skilled artisan in producing a monoclonal antibody other than monoclonal antibody SR-1 that binds the human c-kit receptor and blocks binding of human stem cell factor to the receptor for the treatment of cancer. There is no direction or guidance provided by applicant to assist the skilled artisan in producing a monoclonal antibody that binds a human stem cell factor receptor and blocks the binding of stem cell factor to the receptor. The skilled artisan could not predictably extrapolate the teachings in the specification, limited to the production of monoclonal antibody SR-1 specific for the human c-kit receptor to the production of just any monoclonal antibody that binds to human c-kit and blocks the binding of stem cell factor to the receptor for the treatment of just any cancer. Again, a single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements. *In re Vickers*, 141 F.2d 522, 526-27, 61 USPQ 122, 127 (CCPA 1944); *In re Cook*, 439 F.2d 730, 734, 169 USPQ 298, 301 (CCPA 1971). However, in applications directed to inventions in arts where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims. *In re Soll*, 97 F.2d 623, 624, 38 USPQ 189, 191 (CCPA 1938). In cases

involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *In re Vaeck*, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). This is because it is not obvious from the disclosure of one species, what other species will work.

Based on the evidence regarding each of the *Wands* factors, not solely the presence of a single working example, the specification at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

Applicants' arguments at pp. 7-8 regarding the use of c-kit antibodies to treat solid tumors and leukemia are acknowledged. Applicant refers to the "somewhat ambiguous" role of c-kit in cancer mentioned in the Lennartsson reference as being due to the loss of c-kit expression when certain tumors progress to a malignant phenotype, however, applicant argues that this does not establish that the use of a c-kit antibody to treat cancer is nonenabling since absolute predictability is not required. Applicant also states that one skilled in the art confronted with the potential problems associated with treating solid tumors with an antibody as summarized in Curti and Jain (cited on PTO-892 mailed 2/28/05), would have used antibody fragments having a smaller molecular weight to allow more rapid tumor penetration. Applicants' arguments have been fully considered but are not found persuasive. The claims recite the administration of a monoclonal antibody or fragment thereof and as such encompass the use of a monoclonal antibody for the treatment of just any solid tumor. Thus, applicants' argument that one skilled in the art would use antibody fragments is not commensurate in scope with the claims and does not fully address the enablement of the claimed subject matter. The Federal Circuit has repeatedly held that "the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation'." *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir.

1993). Regarding the unpredictability as it pertains to treating just any solid tumor, the art of Lennartsson indicates that the "somewhat ambiguous" role of c-kit in cancer is due to the loss of c-kit expression when certain tumors progress to a malignant phenotype. The instant application does not characterize the expression of c-kit in solid tumors, which broadly embraces 90% of all cancers, such that one skilled in the art could predictably treat just any solid tumor with a reasonable expectation of success. The examiner acknowledges that absolute predictability is not the standard, however, predictability is one factors considered in determine whether undue experimentation is required. Applicant is reminded that if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling. See, e.g., Chiron Corp. v. Genentech Inc., 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1326 (Fed. Cir. 2004) ("Nascent technology, however, must be enabled with a specific and useful teaching.' The law requires an enabling disclosure for nascent technology because a person of ordinary skill in the art has little or no knowledge independent from the patentee's instruction. Thus, the public's end of the bargain struck by the patent system is a full enabling disclosure of the claimed technology." (citations omitted)).

In view of the lack of the predictability of the art to which the invention pertains as evidenced by Lennartsson et al, Ashman et al, Curti and Jain (all of record), the lack of guidance and direction provided by applicant, and the absence of working examples, undue experimentation would be required to practice the claimed method of inhibiting the growth of just any cancer (i.e., solid tumor) in a patient comprising a monoclonal antibody conjugated to a therapeutic agent wherein the monoclonal antibody binds human c-kit and blocks binding of human stem cell factor with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed cancer therapy and absent working examples providing evidence which is reasonably predictive that the claimed monoclonal antibodies bind human c-kit and block the binding of stem cell factor thereby decreasing the growth rate of just any cancer in a patient, commensurate in scope with the claimed invention.

6. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832.

The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/David J. Blanchard/
Primary Examiner, A.U. 1643